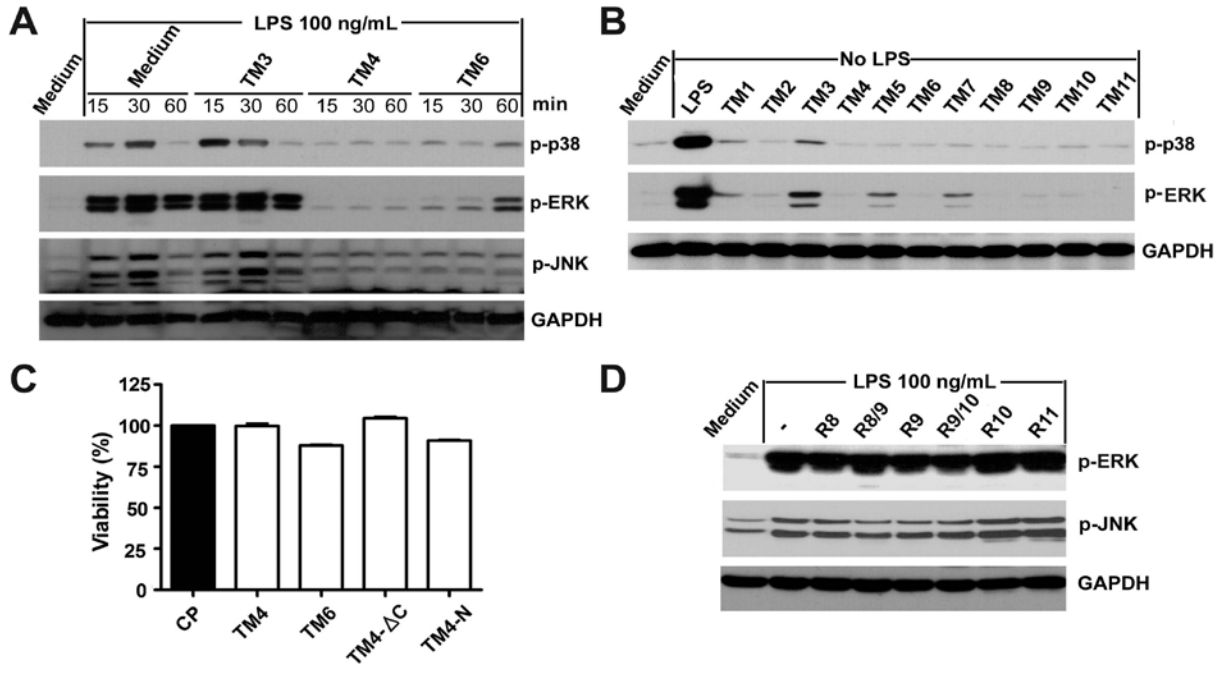
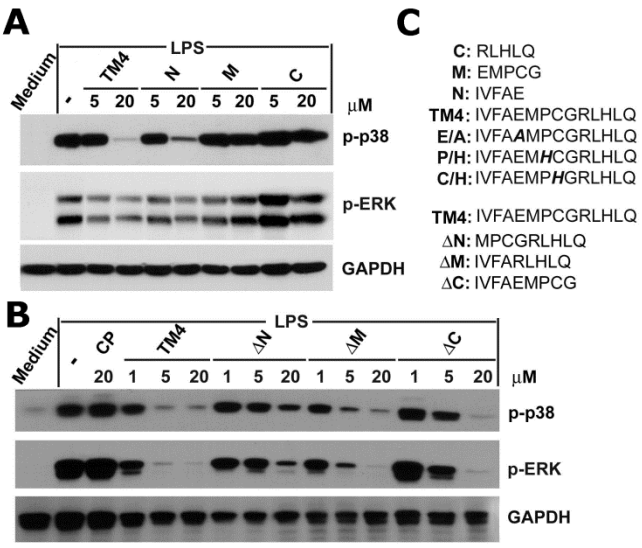
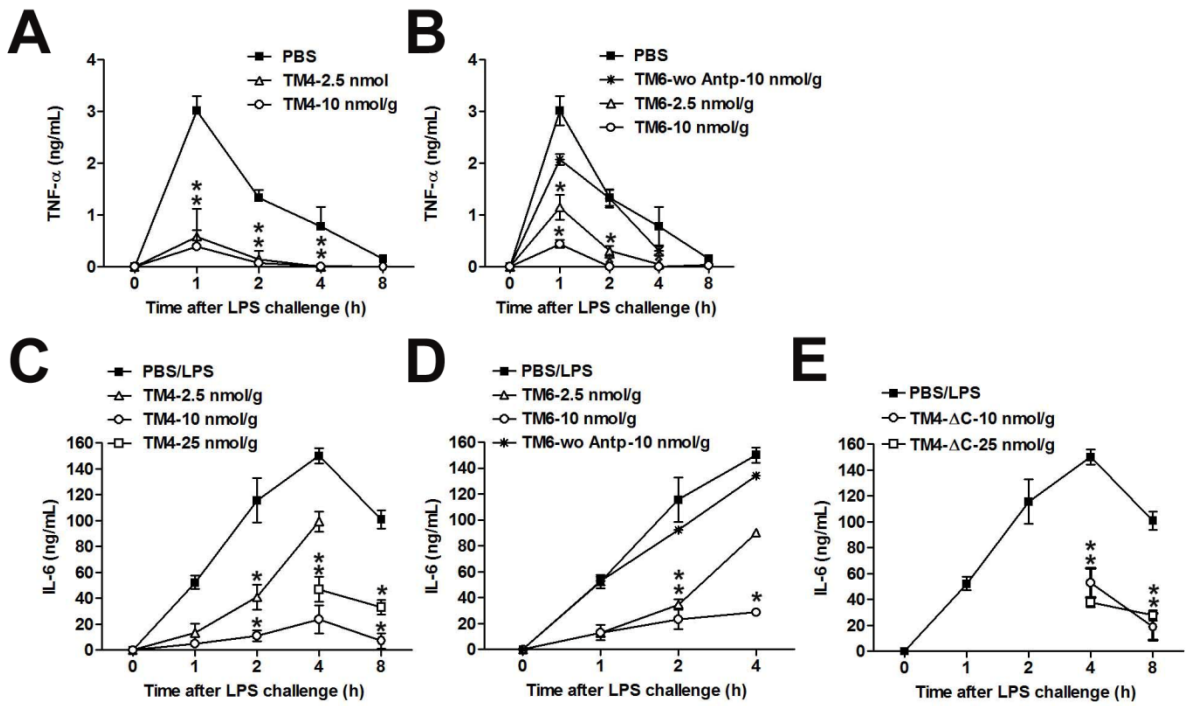
Supplementary Materials



Supplemental Figure S1. (A) TM4 and TM6 inhibit LPS-induced MAPK activation for at least 1 hour. Mouse macrophages were pre-incubated with peptides (20 μM) for 30 min before stimulation with LPS (100 ng/ml) for indicated time. **(B) Effect of TRAM peptides on p38 and ERK phosphorylation.** Mouse macrophages were incubated with a peptide (20 μM) or LPS (100 ng/ml) for 30 min before cell lysis. **(C) Effect of select TRAM peptides on cell viability.** Viability of mouse peritoneal macrophages was determined using MTT incorporation assay. **(D) TM8/9 and TM9/10 peptides do not inhibit LPS-induced ERK and JNK activation.** Mouse peritoneal macrophages were pre-incubated with peptides (20 μM) for 30 min and stimulated with LPS (100 ng/ml) for another 30 min. Data shown are representative of 2 independent experiments.



Supplemental Figure S2. Dose-dependence of TLR4 inhibition by TM4 variants**.** The experimental details are as in Figure 1. Blot shown is a representative of 3 independent experiments (**A, B**). The amino acid sequences of TM4 variants are also shown (**C**).



Supplemental Figure S3. Inhibitory peptides suppress the LPS-elicited *in vivo* inflammatory response in a dose-dependent manner**.** C57BL/6J mice were injected i.p. with 2.5, 10, or 25 nmol/g of animal weight of the indicated peptide 1 h before injection of LPS (1 μg/g). Control mice received PBS only. Blood samples were collected at 0, 1, 2, 4, and 8 h after LPS challenge and TNF-α (**A, B**) and IL-6 (**C**-**E**) were measured by ELISA. TM6 peptide without the cell-permeating sequence (TM6 w/o Antp) was used as a control peptide in this series of experiments. Data represent the means ± s.e.m. of samples collected in at least 3 independent experiments. One and two asterisks marks data that are statistically different from the control group with $p < 0.05$ and $p < 0.01$, respectively (**A**-**E**).